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MICROSTIMULATION OF LUMBOSACRAL SPINAL CORD-MAPPING

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I. Introduction

During this quarter studies examining the hindlimb motor responses to microstimulation of the lumbosacral (L_5, L_6, L_7, and S_1) spinal cord continued. These studies were directed at examining the responses to single electrode mapping of the S_1 and L_7 responses and the correlation of these responses to the histological location of each electrode penetration. The data from L_7 and S_1 are summarized in Figure 1 and 2 and discussed in detail below. In addition, studies using two microelectrodes positioned bilaterally in the L_6 spinal cord to elicit bilateral hindlimb motion were conducted during this quarter. In these studies, left and right hindlimb motion resembling walking, hindquarter lifting, standing, etc., could be produced by focal microstimulation of selected site in the left and right half of the L_6 spinal cord (Figure 3). The results of these studies and methods are discussed in detail below.

II. The Location and Distribution of Motor Responses Elicited by Single Microelectrode Stimulation of the L_7 and S_1 Spinal Cord.

The purpose of these studies was to examine the types of motor responses that can be elicited by microstimulation of the L_7 and S_1 spinal cord and produce a detailed map of these responses by combining responses data with histologically identified electrode position. These studies are similar to those conducted in L_5 and L_6 and present in previous progress reports. The methods used have been described in detail in progress reports 8 and 9, and are similar to those described for two electrode stimulation in the next section of this report. The important methodological points to remember are that: (1) animals are anesthetized and held in a spinal frame. (2) The hindlimb movement is video taped and individual frames are analyzed for changes in position. and (3) The stimulus intensity is increased and decreased slowly over a 2 second period to produce a smooth motion of the hindlimb.

Single electrode focal microstimulation in either L_7 or S_1 spinal cord produced hinblimb motion which involved several groups of muscle and often motion about two or more joints including hip, knee, and ankle joints. Similar to what was seen in L_6 and L_5 the responses in L_7 and S_1 appeared "functional". Hindlimb lifting, extension, and foot placing could be elicited as might occur during standing, walking , or squatting. Figures 1 and 2 plot the locations and distribution of sites tested in the L_7 and S_1 spinal cord and the response elicited at each site. The general terms flexion, extension, adduction, abduction are used in these figures. Flexion consists of lifting of the hindlimb with rotation about the knee and hip joints similar to what might occur with walking or moving into a squatting position. Extension is the downward movement of the hindlimb that might occur with standing or walking. Abduction and adduction are hindlimb movements toward and away from the midline that may occur with turning or balance or position adjustment. In both L_7 and S_1 flexion of the hinblimb is elicited primarily in the dorsal horn and extends a short distance ventral into the intermedial grey (see figure 2). Some of the flexion responses may involve afferent reflex activity initiated by stimulation near afferent inputs to the dorsal horn. Extension was elicited primarily in ventral horn of L_7 and S_1 and extended dorsally to the intermedial grey and medially near the central canal. The activated sites in the ventral horn represent the areas which contain motorneurons, interneurons, as well as axons and other neural processes. Although flexion and extension torque was not measured in these experiments, manual examination of the hindlimb during stimulation suggests that significant force could be generated by stimulation of a single site in the spinal cord. The torque seems large enough to lift and support the cat's hindquarter and lower it in a smooth motion. Figure 1 and 2 also plot the location and distribution of sites which produce abduction or adduction of the left hindlimb. In L_7 the responses are exclusively abduction (Fig 1 right) while in S_1 they are almost exclusively adduction (Fig. 2 right) except for a few sites in the dorsal horn and dorsal columns which elicit abduction.

The sites which elicit adduction/abduction of the hindlimb overlap with those that produce extension. Often single site produces strong extension with some abduction in L_7. This combination of movements may be important in turning and maintaining balance. Those sites in the dorsal horn which produce adduction or abduction may be involved in some type of reflex activity.

These studies should be concluded and published in the next quarter.

III. Bilateral Spinal Cord Microstimulation to Elicit Synchronized Movement of the Hindlimbs.

The purpose of these studies was to examine the possibility of controlling both hindlimbs in a synchronized matter as might occur in walking or standing.

These studies used two electrodes for microstimulation, one in the left and the other in the right side of the spinal cord in order to control both hindlimbs. Stimulus pulses were generated by a computer using 2 channels of an 8 channel D/A (digital to analog) converter. The voltage pulses were passed through constant current isolation units to provide current pulses to two sites in the L_6 spinal cord. Except for the use of two electrode stimulation, the methods were similar to those described in previous progress reports (#8 and #9) and summarized very briefly here.

> Adult male cats are anesthetized with pentobarbital (30-35mg/kg I.V.) and rigidly suspended in a spinal cord frame with the hindlimb allowed to move freely. Reflective markers at each hindlimb joint (hip, knee, and ankle) are video taped using three cameras-one from the left side (for the left hindlimb), one from the right side (for the right hind limb), and a third camera from the back of the hindlimbs. The motion of the hindlimbs generated by spinal cord microstimulation is recorded on video tape and analyzed after completion of the experiment using a computer equipped with a video frame grabber and a CAD (computer aided design) program to measure hindlimb movement on each video frame. Stick figures are generated for each stimulus site from the captured video frames. Spinal cord sites are stimulated every 200 microns along each electrode track and are identified histologically following completion of each experiment. The histological data is then correlated with the motor output generated at each site. The stimulus parameters for mapping studies were 0.2 msec duration charge balanced pulses, 40 Hz at 0-100uA intensity. Pulse intensity was modulated by a sine wave function (see progress report #8 and Fig 4 this report).

Figure 3 illustrates a typical response of the left and right hindlimb generated by left and right spinal cord microstimulation. In this paradigm the left and right spinal cord is stimulated 180° out-of-phase as shown in Fig 4. This produces a lifting of one hindlimb while the other remains extended; followed by lifting of the opposite hindlimb and allowing the other hindlimb to return to its resting or extended position and so on. This sequence produces what apprears to be "walking-like" behavior of the hindlimbs. There seems to be little fatigue that occurs and since the stimulus intensity is increased slowly and decreased slowly (Fig.4) the movement is smooth. The hinblimb movement is however locked to the presentation of stimuli to the spinal cord and does not continue when the stimulation is terminated.

If the spinal cord is stimulated at sites deep in the ventral horn and the stimuli are presented in-phase, extension of both hindlimbs would be elicited as might occur when standing.

Although every site was not examined in detail interactions between the two sites of stimulation were seen. Most often if one side is stimulated at a high intensity for several cycles (15 to 20 seconds) the opposite hindlimb may have a decreased response for several minutes. These responses usual recover and suggest one side of the spinal cord may produce inhibition of the opposite hindlimb response. This interaction can be accounted for by known inhibitory circuits in the spinal cord.

These studies will continue in the next quarter with particular attention to sites which modulate the contralateral hindlimb and the response fatigue that may occur with long duration stimulation.

Figure 1. Drawing of two transverse hemi-sections of the left side of the L_7 spinal cord showing the distribution of sites where microstimulation produces flexion or extension (left hemi-section) or abduction or adduction (right hemi-section) of the left hindlimb of the cat. Stimulation of the left side of the spinal cord produces little or no movement of the right hindlimb. Symbols at bottom of figure represent hindlimb flexion (O), extension (+), abduction (<), adduction (>). Notice that leg lifting or flexion is elicited primarily in the dorsal horn and dorsal part of ventral horn while hindlimb extension is produced in ventral horn and intermediallateral gray area. 645 sites tested in two animals 448 produced responses (64 flexion, 256 extension, 128 abduction, 0 adduction). Several hundred sites were also tested in a third animal and produced similar responses but histology was lost during processing and data could not be plotted.

Figure 2. Same as figure 1 except stimulus sites from S_1 shown. 125 sites were tested in S_1 in one animal 118 sites produced responses. (flexion-45, extension-43, abduction 8, and adduction-22). Several hundred sites were tested in one additional animal with similar responses, but histology was lost during processing and data could not be plotted.

Figure 3. Stick figures of the left and right hindlimbs showing the response elicited by simultaneous microstimulation of two sites, one in the left and the other in the right grey matter of the L_6 spinal cord at a depth of 1.4mm from the spinal cord surface. The stimulus to the right spinal cord was presented 180° out-of-phase with the left cord stimulation (See figure 4). Notice the reciprocal action of the hindlimbs. Left hindlimb is lifted while the right hindlimb is in the extended position. A sequence of this motion on video tape appears as though the animal is walking. The resting position in the absence of stimulation is shown at 0.0 time. Stimulus parameter are 40Hz, 0.2msec pulse duration, 0-100uA stimulus intensity. Stimulus intensity is modulated from 0-100uA by a sine wave function as shown in figure 4.

Figure 4. Schematic drawing showing the stimulus pulses used to activate the left and right side of spinal cord and generate the hindlimb motor responses illustrated in Figure 3. Single negative first pulses at a frequency of 40Hz, and pulses duration of 0.2msec. were used. The pulse amplitude was modulated by a sine wave function as shown in this figure. The stimulus to the left and right side of the spinal cord are 180° out-of-phase to produce the alternating, smooth lifting and lowering of the hindlimb. The duration of the stimulus was a minimum of 4 seconds, although 8, 12, and 16 seconds were also used.

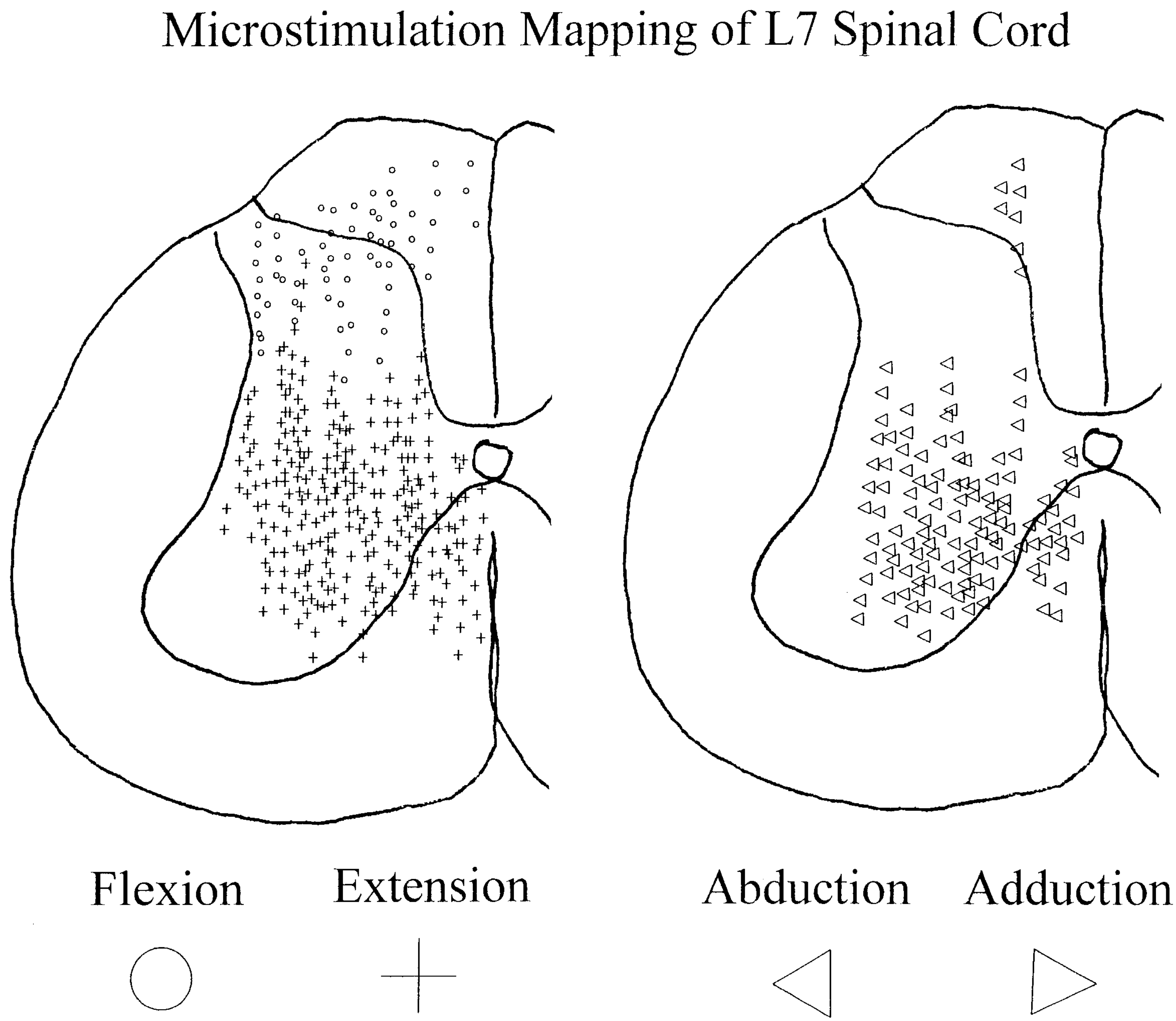
Microstimulation Mapping of L7 Spinal Cord
Flexion
Extension
Abduction
Adduction

Figure 1.

Microstimulation Mapping of S1 Spinal Cord

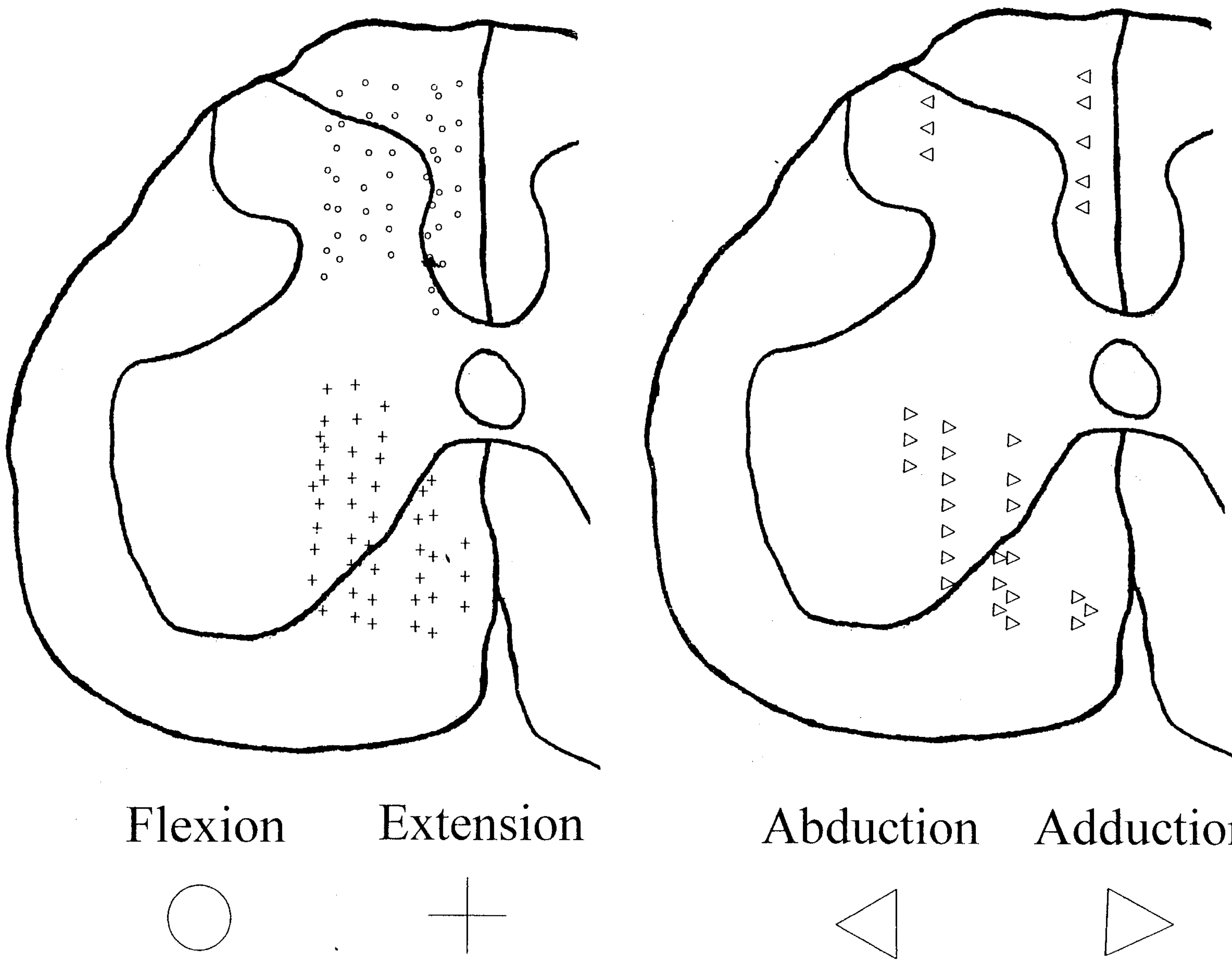

Figure 2.

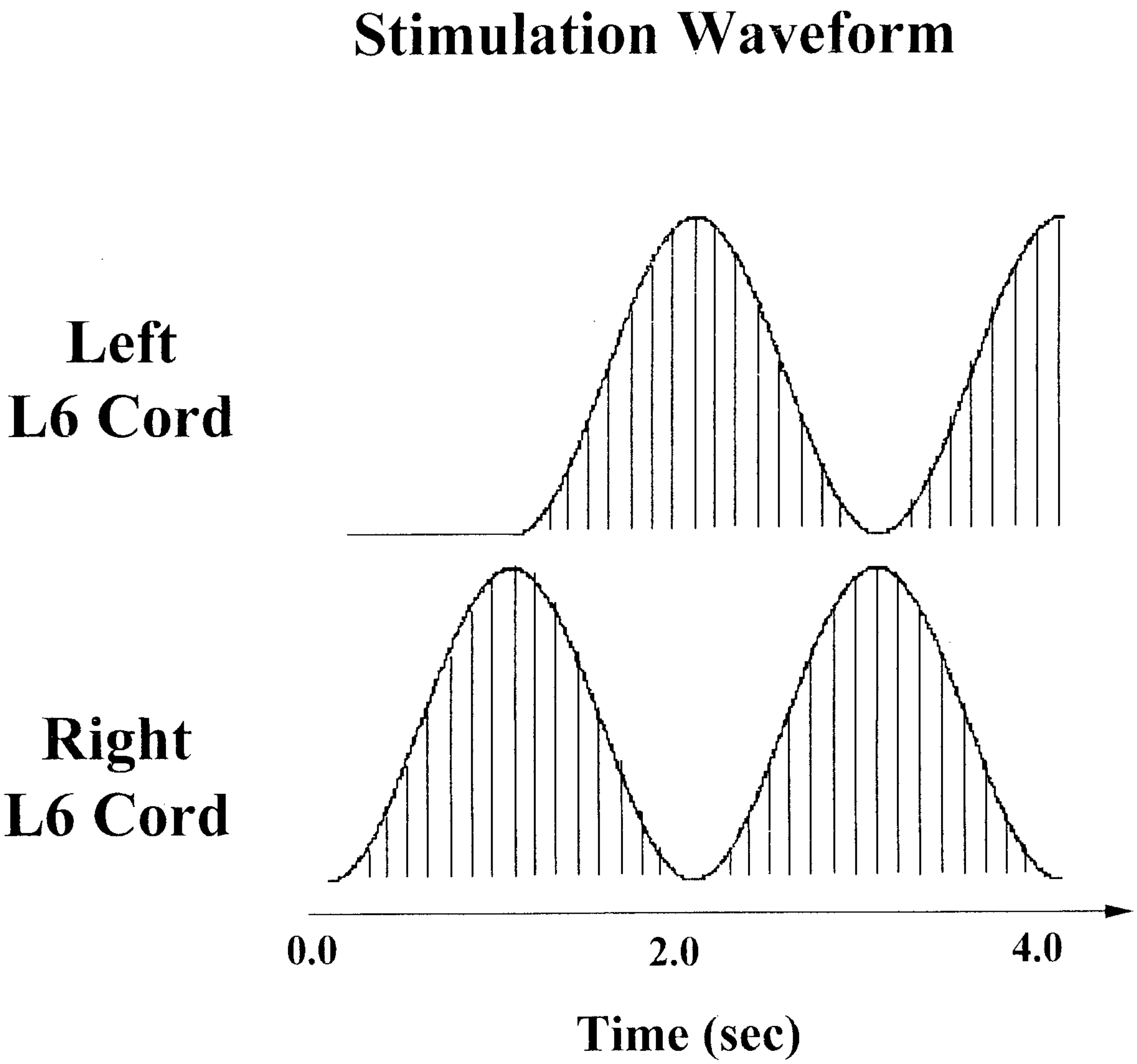
Stimulation Waveform
Left
L6 Cord
Right
L6 Cord
0.0
2.0
4.0
Time (sec)

Figure 4.